Lgr5+ cells regenerate hair cells via proliferation and direct transdifferentiation in damaged neonatal mouse utricle.

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Authors: Tian Wang, Renjie Chai, Grace S Kim, Nicole Pham, Lina Jansson, Duc-Huy Nguyen, Bryan Kuo, Lindsey A May, Jian Zuo, Lisa L Cunningham, Alan G Cheng

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Public Summary:
Recruitment of endogenous progenitors is critical during tissue repair. The inner ear utricle requires mechanosensory hair cells (HCs) to detect linear acceleration. After damage, non-mammalian utricles regenerate HCs via both proliferation and direct transdifferentiation. In adult mammals, limited transdifferentiation from unidentified progenitors occurs to regenerate extrastriolar Type II HCs. Here we show that HC damage in neonatal mouse utricle activates the Wnt target gene Lgr5 in striolar supporting cells. Lineage tracing and time-lapse microscopy reveal that Lgr5+ cells transdifferentiate into HC-like cells in vitro. In contrast to adults, HC ablation in neonatal utricles in vivo recruits Lgr5+ cells to regenerate striolar HCs through mitotic and transdifferentiation pathways. Both Type I and II HCs are regenerated, and regenerated HCs display stereocilia and synapses. Lastly, stabilized -catenin in Lgr5+ cells enhances mitotic activity and HC regeneration. Thus Lgr5 marks Wnt-regulated, damage-activated HC progenitors and may help uncover factors driving mammalian HC regeneration.

Scientific Abstract:
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